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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/648,081	08/25/2000	Guoqing Wang	ART-00101.P.1	4626

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EXAMINER

LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 02/07/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/648,081

Applicant(s)

WANG ET AL.

Examiner

Frank W Lu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 44-48, 53-57 and 64-68 is/are pending in the application.
- 4a) Of the above claim(s) 44-48, 53-56 and 64-68 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 8/25/2000 (original) is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-5 and 57 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that: (1) Groups I through III "are connected by a single searchable unifying relationship" and "share similar method steps that utilize nucleolytic activity and which have been classified by the USPTO in the same class and subclass "; and (2) "[T]he single searchable unifying element can be primarily searched by electronically search key words or, for example, by the common classification".

The above arguments have been fully considered and have not been found pervasive toward the withdrawal of the restriction requirement such that Groups I, II, and III will be examined together. First, Groups I, II, and III were in the same class and subclass was not the reason for the restriction. Second, as shown in previous office action, Groups I, II, and III were distinct and independent inventions since these inventions are directed to methods comprised of different method steps and are required different searches. For example, Group II requires an additional step d) which is not required in Groups I and III while Group III requires a first and a second survey population of nucleic acid molecules which is not required in Groups I and II. Therefore, Groups I through III were not "connected by a single searchable unifying relationship" as suggested by applicant and there would be a search burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL

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Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in People's Republic of China on August 24, 2000. It is noted, however, that applicant has not filed a certified copy of this foreign application as required by 35 U.S.C. 119(b).

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because an alteration in page 3 of the oath or declaration was made without an initial. See 37 CFR 1.52(c).

Drawings

4. The drawings are objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Sequence Rules Compliance

5. This application has complied with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

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Information Disclosure Statement

6. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

7. There is no brief description of the drawings in the specification as required by 37 CFR 1.74.

8. The abstract is not in a single paragraph on a separate sheet within the range of 50 to 250 words.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-5 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claims 2-5 and 57 are dependent on claim 1.

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11. Claim 1 is rejected as vague and indefinite over step(a) of the claims because it is unclear whether a probe-survey population mixture of nucleic acid molecules is a hybridized complex of at least one probe nucleic acid molecule and a survey population of nucleic acid molecules or not. Note that the claim does not require that the probe nucleic acid molecule hybridizes with a survey population of nucleic acid molecules.

12. Claim 1 is rejected as vague and indefinite over the phrase "treating said probe-survey population mixture of nucleic acid molecules with a nucleolytic activity" because it is unclear what is intended. For example, does this phrase mean treating said probe-survey population mixture of nucleic acid molecules with a nuclease or mean something else?

13. Claims 1, 2, and 57 are rejected as vague and indefinite over the phrase "nucleolytic activity-protected nucleic acid molecules" because it is unclear what is intended. For example, does this phrase mean nucleic acid molecules that protect from a nuclease digestion or mean something else? The examiner considered that an enzyme having a nucleolytic activity included protease, which could not digest nucleic acids.

14. Claim 1 is rejected as vague and indefinite over the phrase "nucleolytic activity-sensitive nucleic acid molecules" because it is unclear what is intended. For example, does this phrase mean nucleic acid molecules that are sensitive to a nuclease digestion or mean something else?

15. Claim 1 is rejected as vague and indefinite over step(b) of the claims because it is unclear how "a population of nucleolytic activity-protected nucleic acid molecules" can be generated if said probe-survey population mixture of nucleic acid molecules is DNA or RNA while a nuclease used in the assay is a DNase or a RNase. Please clarify.

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16. Claim 4 is rejected as vague and indefinite over the phrase "nucleolytic activity-resistant linkages" because it is unclear what is intended. For example, does this phrase mean linkages that are resistant to a nuclease digestion or mean something else?

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

18. Claims 1, 2, 4, 5, and 57 are rejected under 35 U.S.C. 102(e) as being anticipated by Kris *et al.*, (US Patent No., 6,238,869, filed on June 21, 1999).

Regarding claims 1, 2, 5, and 57, as shown in Examples 14 and 15, total RNA from mouse liver was mixed with a protection fragment having an oligonucleotide having 70 bp long wherein its 60 bases were complementary to mouse GAPDH. Either a fragment complementary to mouse GAPDH mRNA was used as a protection fragment while its complementary strand was used as a negative control (antisense fragment). RNA samples with protection fragments were heated to 90 °C for 5 minutes, and hybridizations were done by bringing samples to 70 °C and allowing them to cool slowly to room temperature over night as recited in step (a) of claim 1. Then S1 nuclease was added to digest single stranded nucleic acid in RNA-protected fragment complex recited in step (b) of claim 1. Finally, the samples heated to 90 °C for 15 minutes and

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then 37 °C for 15 minutes to denature and destroy RNA recited in claim 2, neutralized with HCl, and incubated on MAPS plates (contained multiple nucleic acid probes) overnight in the presence of biotinylated detection oligonucleotide (considered as a signal nucleic acid molecule) recited in steps (c) and (d) in claim 1, and claims 5 and 57. The amount of signal decreased in parallel with decreasing amounts of mouse RNA (samples included 500, 170, 50, 5, or 0.5 µg of total mouse RNA). Two control samples were included to which no S1 nuclease was added (for examples, see columns 35, 36, 38, and 45-47, and Figures 8, 9, 24, and 25). Note that PNA (peptide nucleic acid) also could be used as a protection fragment recited in claim 4 (see column 30). The peptide region of PNA was considered to be resistant to a nuclease digestion.

Therefore, Kris *et al.*, teach all limitations recited in claims 1, 2, 4, 5, and 57.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

20. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kris *et al.*, (June 21, 1999) as applied to claims 1, 2, 4, 5, and 57 above, and further in view of Tyagi *et al.*, (Nature Biotechnology 14, 303-308, March 1996).

The teachings of Kris *et al.*, have been summarized previously, *supra*.

Kris *et al.*, do not disclose a partial single-stranded nucleic acid probe.

Tyagi *et al.*, teach a hairpin probe having a single-stranded nucleic acid (see abstract in page 303 and Figures 1 and 2 in page 304).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed a method of identifying one or more nucleic acid molecules wherein a hairpin nucleic acid was used as a probe (protection fragment) in view of the reference of Tyagi *et al.*. One having ordinary skill in the art would have been motivated to modify the method of Kris *et al.*, and combine above methods together because the simple replacement of one nucleic acid probe with known properties (i.e., single stranded oligonucleotide) from another nucleic acid probe with known properties (i.e., hairpin probe) in a method of identifying one or more nucleic acid molecules would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their

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expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

21. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Felder *et al.*, (US Patent No. 6,232,066, filed on July 2, 1998).

22. No claim is allowed.

23. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
February 5, 2002


ETHAN C. WHISENANT
PRIMARY EXAMINER